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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/735,608	12/12/2003	Marcel P. Bruchez	IVGN 620.2 CIP	1956

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EXAMINER	
JUNG, UNSU	

ART UNIT	PAPER NUMBER
1641	

MAIL DATE	DELIVERY MODE
09/05/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/735,608	BRUCHEZ ET AL.	
	Examiner	Art Unit	
	UNSU JUNG	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *02 July 2008*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,7,10-13 and 16-43* is/are pending in the application.

4a) Of the above claim(s) *17-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,3,4,6,7,10-13,16 and 38-43* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *12 December 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 2, 2008 has been entered.

The submission included amendments to the specification and claims 1, 16, 42, and 43.

Status of Claims

2. Claims 1, 3, 4, 6, 7, 10-13, and 16-43 are pending, claims 17-37 have been withdrawn from consideration, and claims 1, 3, 4, 6, 7, 10-13, 16, and 38-43 are currently under consideration for patentability under 37 CFR 1.104.

Objections Withdrawn

3. The objection of the specification has been withdrawn in view of amended specification in the reply filed on July 2, 2008.

Rejections Withdrawn

4. The rejection of claims 1, 3, 4, 6, 7, 10, 11, 38, 40, 42, and 43 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement has been withdrawn in view of amended claims 1, 16, and 42 in the reply filed on July 2, 2008.

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

6. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

7. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

8. Claims 1, 3, 4, 6, 7, 10-13, 16, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Science*, 1998, Vol. 281, pp2016-2018) in view of Rothbard et al. (U.S. Patent No. 6,495,663, filed on May 21, 1998).

According to the specification on p14, lines 25-30, the terms "semiconductor nanocrystal," "quantum dot" and "Qdot^{TM} nanocrystal" are used interchangeably herein to refer to semiconductor nanoparticles composed of an inorganic crystalline material that is luminescent (i.e., they are capable of emitting electromagnetic radiation upon excitation), and include an inner core of one or more first semiconductor materials that is optionally contained within an overcoating or "shell" of a second semiconductor material.

Chan et al. teaches highly luminescent semiconductor quantum dots (semiconductor nanoparticles), which are biocompatible and are suitable for use in cell

biology and immunoassays (see entire document, particularly Abstract). The advantages of using semiconductor quantum dots/ nanoparticles over the conventional organic fluorescent dyes are well known in the art. The advantages include resistance to photobleaching and enhanced quantum yield (p2017, Fig. 3 and 3rd column). The improved photostability of the semiconductor quantum dots/ nanoparticles would allow real-time observations of molecular trafficking in living cells (p2017, 2nd column, last paragraph). Further, sufficiently monodispersed semiconductor quantum dots/ nanoparticles would allow use in multiplex detection schemes (p2017, 2nd column, last paragraph).

With respect to claims 3 and 4, Chan et al. teaches a semiconductor nanoparticles comprising CdSe core (Fig. 1).

With respect to claims 6 and 7, Chan et al. teaches a semiconductor nanoparticles comprising ZnS shell (Fig. 1).

With respect to claims 12 and 13, Chan et al. teaches semiconductor nanoparticles comprising CdSe core and ZnS shell (Fig. 1).

However, Chan et al. fails to specifically teach a semiconductor nanoparticle complex, wherein the semiconductor nanoparticle is bound to a cationic polymer comprising of 5 to 25 contiguous Lysine (Lys) and/or Arginine (Arg) residues.

Rothbard et al. teaches methods and composition for transporting drugs and macromolecules across biological membranes wherein the biological membranes are contacted with a conjugate containing a biologically active agent that is covalently attached to a transport polymer (translocatable molecule, see entire document). Such

transport polymer has 5 to 25 subunits of Lys or Arg (SEQ ID NO:'s 2, 3-11 and 13-17). The transport enhancing polymers are exemplified by peptides in which Lys or Arg residues constitute the subunits (SEQ ID NO:'s 2, 3-11 and 13-17). Exemplary eukaryotic cell membranes of interest include membranes of dendritic cells, epithelial cells, endothelial cells, keratinocytes, muscle cells, fungal cells, bacterial cells, plant cells and the like (column 3, lines 17-25). The conjugate is effective to enhance the transport rate of the conjugate across the biological membrane relative to the transport rate of the non-conjugate macromolecules along (column 6, line 63-column 7, line 5). Detecting uptake of macromolecules may be facilitated by attaching a fluorescent tag (see column 11, lines 3-4). Fluorescently labeled peptide polymers composed of 6 or more Arginine residues entered cells more efficiently than the tat sequence 49-57 in Fig. 1 (see column 11, lines 30-40).

With respect to claim 10, Rothbard et al. teaches a cationic polymer having 9 Arg residues (SEQ ID NO: 17).

With respect to claim 11, Rothbard et al. teaches a cationic polymer capable of enhancing the transport across a cell membrane (column 3, lines 17-25 and column 6, line 63-column 7, line 5).

With respect to claim 16, Rothbard et al. teaches a cationic polymer consisting of 6 to 25 contiguous Lys or Arg residues (SEQ ID NO:'s 2, 3-11 and 13-17).

With respect to claims 42 and 43, Rothbard et al. teaches a cationic polymer, which is not a tat peptide, comprising 5 to 25 contiguous Lys and/or Arg residues (SEQ ID NO:'s 1-17).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to employ a cationic polymer consisting of 5 to 25 contiguous Lys or Arg as taught by Rothbard et al. coupled to the semiconductor nanoparticles of Chan et al. in order to transport the semiconductor nanoparticle complex across the biological membrane. The advantage of using cationic polymer, which enhances the transport rate of the semiconductor nanoparticle complex across the biological membrane, provides the motivation to combine teachings of Chan et al. and Rothbard et al. since Chan et al. teaches cell-labeling using semiconductor nanoparticles via receptor-mediated endocytosis (p2018, 1st column) and Rothbard's use of the cationic polymer would facilitate transport across the cell membrane in the endocytosis taught by Chan et al. Further, one of ordinary skill in the art would have had a reasonable expectation of success in employing a cationic polymer consisting of 5 to 25 contiguous Lys or Arg as taught by Rothbard et al. coupled to the semiconductor nanoparticles of Chan et al. since Rothbard et al. teaches that cationic polymer consisting of 5 to 25 contiguous Lys or Arg can be used for transport of conjugates across the biological membrane of eukaryotic and prokaryotic cells.

9. Claims 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. (*Science*, 1998, Vol. 281, pp2016-2018) in view of Rothbard et al. (U.S. Patent No. 6,495,663, filed on May 21, 1998) as applied to claims 1, 10, 12, and 16 above, and further in view of Foster et al. (U.S. Patent No. 4,444,879, Apr. 24, 1984) and Boguslaski et al. (U.S. Patent No. 5,420,016, May 30, 1995).

Chan et al. in view of Rothbard et al. teaches a semiconductor nanoparticle complex as set forth above. However, Chan et al. in view of Rothbard et al. fails to teach that the semiconductor nanoparticle complex is in a kit with instructions for using the semiconductor nanoparticle complex.

Foster et al. teaches a kit comprising reagents for performing an assay and instructions for providing procedure for the use of the kit (see entire document, particularly column 15, lines 30-34).

Boguslaski et al. teaches that a test kit assembled by various system components for conducting assays is more convenient and facile for the test operator (see entire document, particularly column 7, lines 8-11).

Therefore, it would have been obvious to one of ordinary skill in the art at the time of the invention to assemble the components of Chan et al. with instructions for providing procedure for the use of the kit as taught by Foster et al. in order to provide reagents in assembled components for conducting various assays. The advantage of assembling reagents in a kit, which makes its use more convenient and facile for a test operator as taught by Boguslaski et al., provides the motivation to combine teachings of Chan et al. and Foster et al. with a reasonable expectation of success. In addition, the advantage of giving instructions for performing the assay for the user provides the motivation for including instructions of Foster et al. in the composition of Chan et al. with a reasonable expectation of success as the instructions would provide guidelines of how the assay should be performed for the user.

Response to Arguments

10. Rejection of claims 1, 3, 4, 6, 7, 10-13, 16, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Rothbard et al.

Applicant's arguments filed on July 2, 2008 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed herein.

Applicant's argument that Rothbard et al. does not provide a reason to believe its method would work for transport of Chan et al.'s quantum dots across membrane has been fully considered but is not found persuasive. Although Rothbard et al.'s method is limited to transporting macromolecules (molecular weight greater than 1,000 Daltons, column 5, lines 58-61), one of ordinary skill in the art would have had a reasonable expectation of success in transporting quantum dots of Chan et al. since Chan et al. teaches that quantum dots can be transported across cell membrane in intracellular assays using quantum dots as labels for intracellular labeling (p2018, Fig. 4).

Applicant's argument that Rothbard et al. teaches away from attempting to transport Chan et al.'s quantum dot having a hydrophobic coating as Rothbard et al. states that attaching a large hydrophobic moiety may significantly impede or prevent cross-membrane transport has been fully considered but is not found persuasive. The quantum dot of Chan et al. is not hydrophobic as applicant contends. Chan et al. teaches the quantum dots are made water-soluble by attaching polar carboxylic acid groups (p2017, 1st paragraph).

In response to applicant's argument that the references fail to show certain features of applicant's invention, it is noted that the features upon which applicant relies

(i.e., number or ratio of molecules attached to the nanoparticles/selectively attaching one peptide per nanoparticle) are not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Although the claims recite "a semiconductor nanoparticle complex comprising a semiconducting nanoparticle bound to a cationic polymer," the claims do not exclude other unrecited features as the transitional term “comprising” is inclusive or open-ended and does not exclude additional, unrecited elements. See MPEP § 2111.02.

Applicant’s argument regarding multiple polymers being attached to the nanoparticles and their toxicity have been fully considered but is not found persuasive. Although Chan et al. does not provide method of attaching one polymer peptide to the nanoparticle, Rothbard et al. teaches a method of linking one transport polymer via a suitable linking group (column 7, lines 52-57).

Applicant’s argument that there is not evidence to suggest that the transport method of Rothbard et al. would work better than the method of Chan et al. has been fully considered but is not found persuasive essentially for the reasons of record. Chan et al’s method of transport of nanoparticles across cell membrane involves receptor-mediated encocytosis. The transport method of Rothbard et al. does not require specific receptor interaction. Therefore, the transport method of Rothbard et al. is more advantageous than Chan et al.'s method as the transport is independent of presence of transferrin receptor on the cell surface.

In view of the foregoing response to arguments, the rejection of claims 1, 3, 4, 6, 7, 10-13, 16, 42, and 43 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Rothbard et al. has been maintained.

11. Rejection of claims 38-41 under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Rothbard et al., and further in view of Foster et al. and Boguslaski et al.

Applicant's arguments filed on July 2, 2008 have been fully considered but they are not persuasive essentially for the reasons of record and arguments addressed set forth above.

In view of the foregoing response to arguments, the rejection of claims 38-41 are rejected under 35 U.S.C. 103(a) as being unpatentable over Chan et al. in view of Rothbard et al. has been maintained.

Conclusion

12. No claim is allowed.

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to UNSU JUNG whose telephone number is (571)272-8506. The examiner can normally be reached on M-F: 9-5.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on 571-272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Unsu Jung/
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